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N,N-Bis-(quinolin-8-ylmethyl)diaza-18-crown-6 (L) was prepared in a high yield by treating diaza-18-crown-6 with 8-bromomethylquinoline in the presence of triethylamine. Ligand L interacted strongly with Na^+, K^+, Mg^{2+}, Co^{2+}, Cu^{2+}, Ni^{2+}, and Zn^{2+} as shown by calorimetric titration and UV-Visible spectrophotometric tecnhiques. The ligand exhibited a good selectivity for Cu^{2+} over Ni^{2+}. The calorimetric titration indicated that ligand L forms both mononuclear and binuclear complexes with Cu^{2+}.

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Results and Discussion

Synthesis. The synthetic route to ligand 7,16-bis(quinolin-8-ylmethyl)-1,4,10,13-

tetraoxa-7,16-diazacyclooctadecane **L** is depicted in Scheme 1. Intermediate 8-

bromomethylquinoline **(2)** was easily isolated as crystals from EtOH in an 88% yield after the

reaction of 8-methylquinoline **(1)** with NBS in the presence of benzoyl peroxide in refluxing

CCl_4. The reaction of diaza-18-crown-6 with 8-bromomethylquinoline **(2)** in the presence of

Et_3N as base in anhydrous benzene gave **L** in an 87% yield after purification by column

chromatograph on silica gel and recrystallization from CH_2Cl_2/EtOH.

Complexation Thermodynamics. Interactions of **L** with Na^+, K^+, Mg^{2+}, Ba^{2+}, Co^{2+},

Cu^{2+}, Ni^{2+}, and Zn^{2+} were evaluated by calorimetric and UV-visible spectrophotometric

titrations[1-3] in absolute MeOH solution. The values of equilibrium constants (log K) and

enthalpy (ΔH) and entropy changes (TΔS) for these interactions are listed in Table 1. With the

exception of Ni^{2+}, ligand **L** forms stable complexes with the metal ions studied (log $K > 3$). We

first intended to determine the stability constant for the interaction of Ni^{2+} with **L** by the

calorimetric method. The very small reaction heat suggested a weak complexation for which the

log K value cannot be accurately calculated due to insufficient heat. Therefore, we used a

spectroscopic method[38] to evaluate the interaction and obtained a log $K < 1.5$ which is consistent

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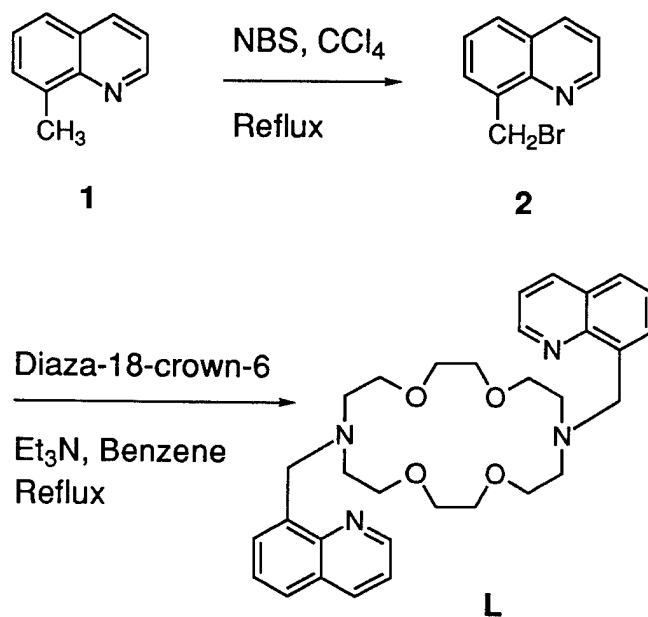
Scheme 1. Syntheses of Bis(quinolin-8-ylmethyl)-substituted ligand **L**

with the calorimetry study. The ligand shows a good selectivity for Cu^{2+} over Ni^{2+} by about three orders of magnitude. Among the metal ions studied, Ba^{2+} forms the most stable complex with the ligand. Selectivity factors for Ba^{2+} over the other cations are more than two orders of magnitude.

The calorimetric titration indicated that ligand **L** forms a binuclear complex with Cu^{2+}. Both 1:1 and 2:1 (Cu^{2+}:L) complexes are observed while all other cations studied form only 1:1 complexes. The data in Table 1 indicate that differences in thermodynamic quantities between 1:1 and 2:1 Cu^{2+}-**L** complexation are small. The binuclear Cu^{2+} complex with a tetraazacrown ether containing two 8-hydroxyquinoline arms has been previously observed in our laboratory.[4] Most of the binuclear Cu(II) complexes reported were formed with all-nitrogen-containing macrocyclic ligands.[5-9] To the best of our knowledge, the Cu(II) complex described in this paper is the first binuclear Cu(II) complex formed with a diaza-18-crown-6 ligand.

It can be seen in Table 1 that entropy effects play a major role in the complexation of Mg^{2+}, Ba^{2+}, and Co^{2+}. The high stability constant of Ba^{2+}-**L** results from both enthalpy and entropy effects. On the other hand, the formation of Mg^{2+} and Co^{2+} complexes is essentially entropy driven.

Experimental Section

Preparation of 8-Bromomethylquinoline (2) (Scheme 1). 8-Bromomethylquinoline was prepared by a similar manner as that described by Kimura et.al.[10] A solution of 8-methylquinoline (**1**) (12.6 g, 88 mmol) in 400 mL of CCl_4 was refluxed with NBS (16.0 g, 90 mmol) in the presence of benzoyl peroxide (0.7 g) for 12 h. The hot solution was filtered and the

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Table 1. Thermodynamic Quantities for the Interactions of Macrocyclic Ligand **L** with Metal Ions in Methanol Solution[a]

cation	$\log K$	ΔH	$T\Delta S$
Na^+	3.73 ± 0.02	-22.5 ± 0.3	-1.2
K^+	4.58 ± 0.03	-39.1 ± 0.3	-13.0
Mg^{2+}	4.02 ± 0.07	9.9 ± 0.6	32.8
Ba^{2+}	6.73 ± 0.08 [c]	-19.4 ± 0.4 [c]	19.0
Co^{2+}	3.21 ± 0.06	14.4 ± 0.8	32.7
$Cu^{2+}(1)$[b]	4.43 ± 0.04	-35.7 ± 0.5	-10.4
$Cu^{2+}(2)$[b]	4.15 ± 0.04	-32.8 ± 0.6	-9.11
Ni^{2+}	< 1.5		
Zn^{2+}	3.66 ± 0.08		

[a] Both ΔH and $T\Delta S$ values are in kJ/mol. Except Cu^{2+}, all thermodynamic parameters are for 1:1 interactions. The $\log K$ values for Ni^{2+} and Zn^{2+} interactions were evaluated at 23 °C by UV-visible spectrophotometric titrations and other $\log K$ values were determined at 25 °C by calorimetric titrations.

[b] Thermodynamic parameters for $Cu^{2+}(1)$ and $Cu^{2+}(2)$ refer to the formation of 1:1 complex Cu^{2+}L and 2:1 complex $(Cu^{2+})_2$L (from Cu^{2+} and Cu^{2+}L), respectively.

[c] Determined by a competitive calorimetric titration.

brown filtrate was evaporated under reduced pressure. The residue was dissolved in 50 mL of CHCl$_3$, and the solution was washed twice with saturated aqueous Na$_2$CO$_3$ and once with water. The organic phase was dried (Na$_2$SO$_4$) and evaporated. The residue was recrystallized from EtOH to give 17.2 g (88%) of **2** as white crystals. The mp and NMR spectral data were identical to those reported.[10]

7,16-Bis(quinolin-8-ylmethyl)-1,4,10,13-tetroxa-7,16-diazacyclooctadecane monohydrobromide (L) (Scheme 1). A solution of **2** (2.0 g, 9.0 mmol) in 50 mL of benzene was added dropwise to a solution of diaza-18-crown-6 (1.0 g, 3.8 mmol) and Et$_3$N (1.6 g, 15.8 mmol) in 50 mL of benzene under N$_2$. The mixture was stirred at room temperature for 20 h and then refluxed for 2 h. The solvent was evaporated under reduced pressure. The residue was treated with a mixture of water and CHCl$_3$ (1:2). The organic layer was separated, washed with water, and dried (Na$_2$SO$_4$). After evaporation, the residue was purified by column chromatography on silica gel with acetone as eluent. The product was recrystallized from CH$_2$Cl$_2$/EtOH to give 1.81 g (87%) of **L·HBr** as yellow crystals, mp 95-96 °C; ^{1}H NMR: δ 2.93. (t, 8H), 3.66 (m, 16H), 4.43 (S, 4H), 7.36 (dd, 2H), 7.52 (d, 2H), 7.65 (dd, 2H), 8.02 (d, 2H), 8.11 (dd, 2H), 8.90 (dd, 2H); ^{13}C NMR (CDCl$_3$): δ 54.78, 54.86, 70.33, 71.00, 120.95, 126.53, 126.74, 128.36, 129.20, 136.54, 138.23, 147.02, 149.42; HRMS: m/z calcd. for C$_{32}$H$_{41}$O$_4$N$_4$ (M+H)$^+$: 545.3130, found: 545.3132. Anal. Calcd for C$_{32}$H$_{40}$N$_4$O$_4$·CH$_2$Cl$_2$·H$_2$O: C, 61.20; H, 6.85. Found: C, 61.24; H, 6.62.

Calorimetric Measurements. Values of log K, ΔH, and TΔS for the interactions of metal ions (except Ni^{2+} and Zn^{2+}) with **L** were determined as described earlier[1] in absolute MeOH

solutions at 2.50 ± 0.1 °C by titration calorimetry using a Tronac Model 450 calorimeter equipped with a 20-mL reaction vessel. The metal ion solutions were titrated into the macrocyclic ligand solutions and the titrations were carried out to a 2-fold excess of metal ions. In general, concentrations of the ligands were $(2.2 - 3.2) \times 10^{-3}$ M and those of the metal ions 7.5×10^{-2} M (K^+) - 0.1 M. In the case of Cu^{2+}, concentration of the ligand was 1.5×10^{-3} M and that of Cu^{2+}, 5.1×10^{-2} M. After a 2:1 (Cu^{2+}:L) complex was observed, the Cu^{2+} concentration was increased to 0.11 M. The method used to process the calorimetric data and to calculate the log K and ΔH values has been described.[2] Calorimetric titrations showed no detectable heat for the Ni^{2+}-L interaction and a white precipitate was observed when the ligand ($(1.5 - 2.1) \times 10^{-3}$ M) was titrated with Zn^{2+}. Therefore, log K values for Ni^{2+} and Zn^{2+} interactions were evaluated by a UV-visible spectrophotometric method.

UV-Visible Spectral Measurements. UV-visible spectra were recorded at 23 ± 1 °C in a 1-cm quartz cell by using a Hewlett-Packard 8453 spectrophotometer. Absolute MeOH was used as the solvent. For the determination of stability constants, a 5.0×10^{-5} M L solution (2.50 mL) was titrated by Ni^{2+} or Zn^{2+} solution and the UV-visible spectra were recorded after each titration. The method described by Bourson and Valeur[3] was employed to calculate log K values. Absorbence data at 280 and 284 nm were used to make the calculations for L-Zn^{2+} and L-Ni^{2+} interactions respectively. Since nickel nitrate showed a weak absorption at 284 nm in MeOH solution ($\varepsilon = 10.9$ $M^{-1}cm^{-1}$), the values of ligand absorbance were corrected by subtracting the Ni^{2+} absorption.

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